App. No. 10/579,106 Filed February 16, 2007 Reply to Office Action of March 4, 2009

## AMENDMENTS TO THE CLAIMS

Attorney Docket No.: 11808-038-999

CAM No.: 120024-999038

This Listing of the Claims will replace all prior versions, and listings, of claims in the application:

## Listing of Claims

- 1-129 (Cancelled).
- 130. (Withdrawn) A process useful for forming enantiomerically-enriched tetrahydrobiopterin (BH4) or a salt thereof from neopterin, comprising the steps of:
- (a) reacting the primary hydroxyl group of neopterin with a silyl protecting group to form a silyl ether;
- (b) protecting at least one secondary hydroxyl group of neopterin with at least one secondary hydroxyl-protecting group;
- (c) converting the silyl ether formed in step (a) to a surrogate group selected from the group consisting of halogens, sulfonates, and thioethers;
  - (d) reducing the surrogate group of step (c) to a methyl group; and
  - (e) removing the secondary hydroxyl-protecting group(s) added in step (b).
- 131. (Withdrawn) The process of claim 130, further comprising the steps of protecting the primary amine group at C-2 of neopterin with a 2-amino protecting group before performing step (a) and removing the 2-amino protecting group after performing step (a).
- 132. (Withdrawn) The process of claim 131, wherein the 2-amino protecting group comprises a dialkylformamidedialkylacetal group or a pivaloyl derivative of neopterin.
- 133. (Withdrawn) The process of claim 132, wherein the dialkylformamidedialkylacetal group is selected from the group consisting of *N*,*N*-dimethylformamidediethylacetal and *N*,*N*-dimethylformamidedimethylacetal.
- 134. (Withdrawn) The process of claim 130, wherein the neopterin of step (a) comprises a compound of formula 20:

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$$\begin{array}{c|c} R_5O & O & OH \\ \hline R_5O & N & N & \tilde{O}H \\ \hline R_6 & \tilde{O}H & \mathbf{20} \end{array}$$

wherein R<sub>5</sub> is -COR';

R' is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, an aryl group, and *t*-butyl; and

R<sub>6</sub> is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, and an aryl group.

- 135. (Withdrawn) The process of claim 130, wherein said silyl protecting group of step (a) is selected from the group consisting of a linear chain alkyl substituted silyl group, a branched chain alkyl substituted silyl group, and an aryl substituted silyl group.
- 136. (Withdrawn) The process of claim 135, wherein said silyl protecting group comprises a *t*-butyldimethylsilyl group or a *t*-butyldiphenylsilyl group.
- 137. (Withdrawn) The process of claim 130, wherein at least one secondary protecting group comprises an acetal or a ketal.
- 138. (Withdrawn) The process of claim 137, wherein the ketal comprises isopropylideneketal.
- 139. (Withdrawn) The process of claim 130, wherein the surrogate group comprises a halogen, and wherein the converting of step (c) comprises reacting the silyl ether and a triphenylphosgine halogen.
- 140. (Withdrawn) The process of claim 130, wherein the surrogate group comprises a sulfonate, and wherein the converting of step (c) comprises removing the silyl ether to form a primary hydroxyl group and sulfonating the resulting primary hydroxyl group.
- 141. (Withdrawn) The process of claim 130, wherein the surrogate group comprises a thioether, and wherein the converting of step (c) comprises reacting the silyl ether and a mixture of (1) triphenylphosphine, (2) a dialkyl azodicarboxylate, and (3) a thiol.

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142. (Withdrawn) The process of claim 130, wherein the reducing of step (d) comprises reacting the surrogate of step (c) and a reducing agent comprising (1) Raney nickel and hydrogen or (2) sodium borohydride.

- 143. (Withdrawn) The process of claim 130, further comprising the step of: (f) performing an erythro-selective reduction of the product of step (e) to form BH4 or a salt thereof.
- 144. (Withdrawn) The process of claim 143, further comprising (g) crystallizing the BH4 salt.
  - 145. (Withdrawn-currently amended) A compound having a formula:

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wherein R<sub>1</sub> is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethyleneimine group, a single branched chain alkyl substituted alkylaminomethyleneimine group, a double linear chain alkyl substituted alkylaminomethyleneimine group, and a double branched chain alkyl substituted alkylaminomethyleneimine group;

R<sub>2</sub> is a silyl group that is stable under acidic conditions;

R<sub>3</sub> is selected from the group consisting of NH<sub>2</sub>, 2,2-dimethylpropanamide, a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an single substituted amino group, a linear chain alkyl substituted sulfur group, and a branched chain alkyl substituted sulfur group;

R<sub>4</sub> comprises a substituted acetal or ketal group that is stable under alkaline conditions; R<sub>5</sub> is a halogen;

R<sub>6</sub> is selected from the group consisting of a linear chain alkyl substituted sulfonate, a branched chain alkyl substituted sulfonate, and an aryl substituted sulfonate; and R<sub>7</sub> is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl group, and an aryl group.

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146. (Withdrawn) The compound of claim 145, wherein R<sub>2</sub> is selected from the group consisting of diethylisopropylsilyl, dimethylisopropylsilyl, dimethylphenylsilyl, diphenylisopropoxysilyl, diphenyl-t-butoxysilyl, di-*t*-butylmethylsilyl, di-*t*-butylsilylene, methyldiisopropylsilyl, methyldiphenylsilyl, *t*-butylmethoxyphenylsilyl, *t*-butyldimethylsilyl, thexyldimethylsilyl, triethylsilyl, 1,1,3,3,-tetra-isopropyldisiloxane, triisopropylsilyl, trimethylsilyloxycabomyl, and *t*-butyldiphenylsilyl.

- 147. (Withdrawn) The compound of claim 145, wherein R<sub>4</sub> is selected from the group consisting of methylene acetal, ethylidene acetal, *t*-butylmethylidene ketal, 1-*t*-butylethylidene ketal, 1-phenylethylidene ketal, 1-(4-methoxyphenyl)ethylidene acetal, 2,2,2-trichloroethylidene acetal, acrolein acetal, cyclopentylidene ketal, cyclohexylidene ketal, cycloheptylidene ketal, benzylidene acetal, p-methoxybenzylidene acetal, 2,4-dimethoxybenzylidene acetal, 2-nitrobenzylidene acetal, 4-nitrobenzylidene acetal, mesitylene acetal, 1-naphthaldehyde acetal, benzophenone ketal, and isopropylideneketal.
- 148. (Withdrawn) The compound of claim 145, wherein  $R_6$  comprises a tosyl group.
- 149. (Withdrawn) A process for forming enantiomerically-enriched tetrahydrobiopterin (BH4) or a salt thereof from a pterin, comprising the steps of:
  - (a) substituting a pterin at the C-6 position to form a 6-substituted pterin;
- (b) protecting the primary amine group at C-2 of the 6-substituted pterin with an amino protecting group;
- (c) reacting the protected 6-substituted pterin of step (b) and a metalation reagent to form a metalation intermediate;
- (d) reacting the metalation intermediate and a lactic acid or a precursor of lactic acid;
  - (e) removing the 2-amino protecting group of the product of step (d); and
  - (f) performing an erythro-selective reduction to form BH4 or a salt thereof.
- 150. (Withdrawn) The process of claim 149, wherein the 6-substituted pterin comprises a 6-halogenated pterin or a 6-sulfonated pterin.

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151. (Withdrawn) The process of claim 149, wherein the amino protecting group is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a linear chain alkyl single substituted amido group, a branched chain alkyl single substituted amido group, and an aryl substituted amido group.

- 152. (Withdrawn) The process of claim 149, wherein the amino protecting group is selected from the group consisting of N,N-dimethylformamidediethylacetal, N,N-dimethylformamidedimethylacetal, and bis-dimethylamino-alkoxymethane.
- 153. (Withdrawn) The process of claim 149, wherein the metalation reagent is selected from the group consisting of RMgX, an alkyl-metal complex, and a metal, wherein X is a halogen, and R is selected from the group consisting of an alkyl group and an aryl group.
- 154. (Withdrawn) The process of claim 153, wherein the metalation reagent is isopropyl magnesium chloride or an alkyl lithium complex.
- 155. (Withdrawn) The process of claim 149, wherein the lactic acid of step (d) comprises a hydroxyl protected lactic acid chloride or the precursor of lactic acid of step (d) comprises 2-oxopropanoyl chloride or 2-oxopropanal.
- 156. (Withdrawn) The process of claim 149, wherein the erythro-selective reduction comprises using (1) sodium borohydride in an alkaline medium or (2) hydrogen and a catalytic amount of platinum dioxide.
- 157. (Withdrawn) The process of claim 149, further comprising the step of: (g) crystallizing the BH4 salt.
  - 158. (Withdrawn-currently amended) A compound [[of]] having a formula:

$$\begin{array}{c}
OR_2 \\
N \\
N
\end{array}$$
or

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$$\begin{array}{c}
OR_2 \\
N \\
N \\
N
\end{array}$$
N
$$M$$
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wherein X is selected from the group consisting of chlorine, bromine, iodine, and a sulfonate;  $R_1$  is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethylene-imine group, a double linear chain alkyl substituted alkylaminomethylene-imine group, and a double branched chain alkyl substituted alkylaminomethylene-imine group;

R<sub>2</sub> is selected from the group consisting of hydrogen, a linear chain alkyl group, a branched chain alkyl group, and an aryl group; and

M is selected from the group consisting of boron, silicon, zirconium, titanium, sodium, aluminum, nickel, cobalt, scandium, chromium, ytterbium, lithium, magnesium, zinc, palladium, copper, manganese, cesium, and tin.

- 159. (Withdrawn) The compound of claim 158, wherein R<sub>1</sub> comprises an *N*,*N*-dimethylaminomethylene substituted amino group.
  - 160. (Withdrawn) A compound having a formula:

$$\begin{array}{c|c} OR_2 & O \\ HN & \tilde{O}R_3 \\ \hline \\ R_1 & N & \tilde{O}R_3 \\ \hline \\ H_2N & N & \tilde{O}R_3 \\ \hline \end{array}$$
 or

wherein R<sub>1</sub> is selected from the group consisting of NH<sub>2</sub>, 2,2-dimethylpropanamide, a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, a double branched chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, and a branched chain alkyl substituted sulfur group;

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R<sub>2</sub> is selected from the group consisting of hydrogen, a linear chain alkyl group, a branched chain alkyl group, and an aryl group; and R<sub>3</sub> is an acyl group.

- (Currently Amended) A process useful for forming enantiomerically-161. enriched tetrahydrobiopterin (BH4) or a salt thereof from neopterin, comprising the steps of:
- (a) protecting the primary amine group at C-2 of neopterin with an amino protecting group;
  - (b) converting the primary hydroxyl group of neopterin to a thioether; and
  - (c) reducing the thioether of step (b) to a methyl group.
- 162. (Currently Amended) The process of claim 161, wherein step (c) simultaneously further comprises removing also results in removal of the primary amine protecting group and performing an erythro-selective reduction to form BH4 or a salt thereof.
- 163. (Previously Presented) The process of claim 162, wherein the erythroselective reduction comprises using Raney nickel and hydrogen.
- 164. (Previously Presented) The process of claim 161, further comprising the step of removing the primary amine protecting group after step (c).
- 165. (Previously Presented) The process of claim 164, wherein the removing comprises reacting with zinc dichloride in ethanol.
- 166. (Previously Presented) The process of claim 164, further comprising the step of performing an erythro-selective reduction to form BH4 or a salt thereof.
- 167. (Previously Presented) The process of claim 166, wherein the erythroselective reduction comprises using (1) sodium borohydride in an alkaline medium or (2) hydrogen and a catalytic amount of platinum dioxide.
  - 168. (Withdrawn) A compound having a formula:

$$\begin{array}{c|c}
O & OH \\
HN & S & R_2 \\
R_1 & N & OH \\
\hline
OH & S & R_2
\end{array}$$
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wherein R<sub>1</sub> is selected from the group consisting of a single linear chain alkyl substituted amino group, a single branched chain alkyl substituted amino group, a double linear chain alkyl substituted amino group, an aryl single substituted amino group, a linear chain alkyl substituted sulfur group, a branched chain alkyl substituted sulfur group, a single linear chain alkyl substituted alkylaminomethyleneimine group, a single branched chain alkyl substituted alkylaminomethyleneimine group, a double linear chain alkyl substituted alkylaminomethyleneimine group, and a double branched chain alkyl substituted alkylaminomethyleneimine group; and a double branched chain alkyl substituted alkylaminomethyleneimine group; and

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R<sub>2</sub> is selected from the group consisting of a linear chain alkyl group, a branched chain alkyl groups, and an aryl group.